Research Letter:

Assessing the public health relevance of a risk factor

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Abstract

In a recent series of high impact public health publications, the c-index was used as measure of prediction to assess the public health relevance of a risk factor. I demonstrate that the c-index is an inferior measure as compared to the classical epidemiologic measures most commonly employed for risk prediction and public health assessment such as disease incidence, relative risk (RR), and population-attributable risk (PAR). I recommend using the latter measures when assessing the public health relevance of a risk factor.

Keywords: Risk factor prevalence, disease incidence, relative risk, population-attributable risk, c-index.

In a recent series of high impact public health publications [1–4], the c-index [5] was used as measure of prediction to assess the public health relevance of a risk factor. In the following, I demonstrate that the c-index is an inferior measure to the classical epidemiologic measures most commonly employed for risk prediction such as disease incidence, relative risks (RR) and population-attributable risks (PAR). Let us use the following notation: $p_0 =$ disease incidence among those not exhibiting the risk factor, $p_1 =$ disease incidence among those exhibiting the risk factor, RR $= p_1/p_0 =$ relative risk associated with the risk factor, $f =$ risk factor prevalence, $f_{\text{cases}} = f\,p_1/[f\,p_1 + (1-f)\,p_0] =$ risk factor prevalence among (future) cases, $f_{\text{controls}} = f\,(1-p_1)/[f\,(1-p_1) + (1-f)\,(1-p_0)] =$ risk factor prevalence among (future) controls, PAR $= f\,(\text{RR}-1)/[f\,(\text{RR}-1)+1] =$ population-attributable risk. The c-index

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expresses the probability of successfully identifying the (future) case and the (future) control among a randomly selected pair consisting of a (future) case and a (future) control by a strategy predicting that every subject exhibiting the risk factor is a case and every subject not exhibiting the risk factor is a control. Because that strategy has a probability of success of 0.5 if both of the selected pair exhibit or do not exhibit the risk factor, the c-index formula is given by

$$\begin{aligned}\text{c-index} = {} & 0.5 \times \text{probability of the selecting a case and a control both exhibiting the risk factor} \\ & + 0.5 \times \text{probability of the selecting a case and a control both not exhibiting the risk factor} \\ & + 1 \times \text{probability of the selecting a case and a control where the case exhibits the risk} \\ & \quad \text{factor and the control does not.}\end{aligned}$$

If we re-write that formula using f_{cases} and f_{controls}:

$$\begin{aligned}\text{c-index} &= 0.5 \times f_{\text{cases}} \times f_{\text{controls}} + 0.5 \times (1 - f_{\text{cases}}) \times (1 - f_{\text{controls}}) + 1 \times f_{\text{cases}} \times (1 - f_{\text{controls}}) \\ &= 0.5 \times (1 + f_{\text{cases}} - f_{\text{controls}}),\end{aligned}$$

we discover a linear increase in the c-index with increasing difference in risk factor prevalence among cases and controls. If the risk factor prevalence in the population is fixed, then the c-index increases with increasing RR or increasing disease incidence. Figure 1 demonstrates that, in the common epidemiologic scenario of a disease incidence among those not exhibiting the risk factor of less than 10 percent and of an RR associated with the risk factor of 1.5, a risk factor prevalence of 20 percent or 50 percent would imply a substantial PAR of 9 percent or 20 percent, respectively, but a poor c-index not exceeding 0.55 or 0.56, respectively. This demonstrates that the c-index is an inferior measure of public health relevance to the combination of disease incidence, relative risk, and population-attributable risk. I therefore recommend using the latter measures to assess the public health relevance of a risk factor.

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Figure 1: Contour plot of the c-index in dependence of the risk of disease among people not exposed to a specific risk factor and the relative risk (RR) - or alternatively the population-attributable risk (PAR) - of disease associated with that risk factor when the prevalence of the risk factor in that population is (a) 50 percent, (b) 20 percent, or (c) 10 percent.